

*RENAME -

5HT_{2A} 10/622,055

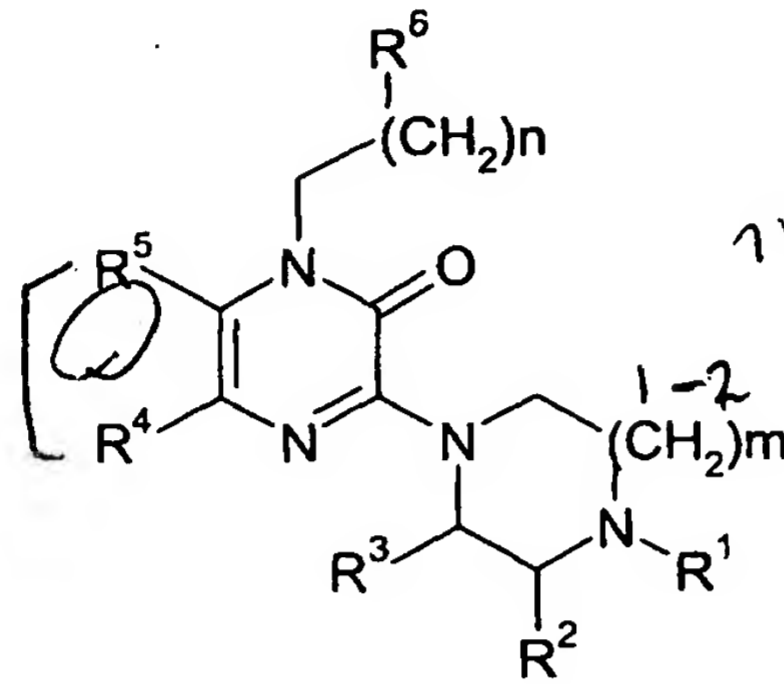
RECEPTOR
ANTAGONISTS

SWEDISH PRIORITY
7/19/02

USPD. 4/14/02
60/426,240

CLAIMS

1. A compound of the general formula (I):



7 MEMBERED - DIAZEPINE
OR
6 MEMBERED - PIPERAZINE

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(I)

5

wherein

m is 1 or 2;
n is 0, 1, 2, 3 or 4;

R¹ is H, C₁₋₆-alkyl, aryl-C₁₋₃-alkyl, heteroaryl-C₁₋₃-alkyl, 2-hydroxyethyl, methoxy-C₂₋₄-alkyl, C₁₋₄-alkoxycarbonyl, aryloxy-C₂₋₃-alkyl, or heteroaryloxy-C₂₋₃-alkyl; wherein

10

any aryl or heteroaryl residue may be substituted with C₁₋₄-alkyl, C₁₋₄-alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano;

R² and R³ each, independently, represent H or CH₃;

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R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1H-quinoxalin-2-one nucleus; and

R⁶ represents aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, heteroaryl-NH, aryl, arylcarbonyl, heteroaryl, or heteroarylcarbonyl;

20

wherein

any aryl or heteroaryl residue, alone or as part of another group, may be unsubstituted or substituted with one, two, three, four or five substituents, independently selected from aryl, aryl-C_{1,2}-alkyl, arylcarbonyl, heteroaryl, heteroaryl-C_{1,2}-alkyl, heteroarylcarbonyl,

5HT_{2A} ANTAGONISTS
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aryloxy, heteroaryloxy, arylthio, heteroarylthio, arylamino, heteroarylamino, C₃₋₆-cycloalkyl, C₃₋₆-cycloalkyloxy, C₃₋₆-cycloalkylcarbonyl, C₁₋₆-alkyl, C₂₋₆-alkanoyl, C₂₋₆-alkynyl, C₂₋₆-alkenyl, or fluoro-C₂₋₄-alkyloxy, halogen, trifluoromethyl, nitro, cyano, trifluoromethoxy, trifluoromethylthio, C₁₋₆-alkoxy, C₁₋₆-alkylthio, C₁₋₆-alkylamino, C₁₋₄-dialkylamino, hydroxy or oxo; wherein

any aryl or heteroaryl residue as substituents on aryl or heteroaryl, alone or as part of another group, in turn may be substituted in one or more positions, independently of each other, by C₁₋₄-alkyl, C₁₋₄-alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano;

and pharmaceutically acceptable salts, hydrates, geometrical isomers, tautomers, optical isomers, N-oxides and prodrug forms thereof, with the provisos that:

R² and R³ are not both CH₃;

when n = 1 and R¹, R², R⁴ and R⁵ are H and R³ is H or CH₃, then R⁶ is not 3-pyridyloxy, 6-methyl-2-nitro-3-pyridyloxy, or 2-chloro-3-pyridyloxy;

when n = 0, then R⁶ is not aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH or heteroaryl-NH; and

the compound of formula (I) is not 1-benzyl-3-(4-methyl-piperazin-1-yl)-1*H*-quinoxalin-2-one.

2. The compound according to claim 1, wherein any aryl or heteroaryl residue, alone or as part of another group, is substituted with one or two non-halogen substituents.
3. The compound according to claim 1, wherein any aryl or heteroaryl residue, alone or as part of another group, is substituted with at least one halogen substituent.

4. The compound according to claim 1 or 2, wherein any aryl or heteroaryl residue that is a substituent on another aryl or heteroaryl, alone or as part of another group, in turn is substituted in one position.

5. The compound according to claim 1, wherein

$n = 1$;

R^1, R^2, R^3, R^4 and R^5 each are H; and

R^6 is phenoxy, where the phenyl ring of the said phenoxy group may be unsubstituted or substituted with one, two, three, four or five substituents.

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6. The compound according to claim 5, wherein the phenyl ring of R^6 is substituted with one, two, three, four or five substituents independently selected from

halogen,

15

2-propenyl,

C_1 - C_6 -alkyl,

C_1 - C_6 -alkoxy,

trifluoromethyl,

phenyl,

20

phenoxy,

benzoyl, and

C_3 - C_6 -cycloalkyl;

25

wherein the phenyl, phenoxy or benzoyl substituent in turn may be unsubstituted or substituted in one or more positions, independently of each other, by C_{1-4} -alkyl, C_{1-4} -alkoxy, C_{1-4} -alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano.

7. The compound according to claim 6, wherein the phenyl ring of R^6 is substituted with one or two non-halogen substituents.

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8. The compound according to claim 6, wherein the halogen substituent is fluorine.

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9. The compound according to claim 1, wherein
n = 1;
R¹ is methoxy-C₂-C₄-alkyl or straight-chained C₁-C₄-alkyl;
R², R³, R⁴ and R⁵ each are H; and
5 R⁶ is 2,4,5-trifluorophenoxy.
10. The compound according to claim 1, wherein
n = 1;
R¹, R², R³, R⁴ and R⁵ each are H; and
10 R⁶ is 2-oxo-1,3-benzoxathiol-5-yloxy.
11. The compound according to claim 1 wherein
n = 0;
R¹, R², R³, R⁴ and R⁵ each are H; and
15 R⁶ is phenyl, where the said phenyl may be substituted with halogen,
in one, two, three, four or five positions.
12. The compound according to claim 11 wherein the halogen is fluorine.
- 20 ~~13~~¹⁴ The compound according claim 1, which is:
- 1-[2-(2-fluoro-4-nitrophenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 1-{2-[(2-oxo-2H-chromen-7-yl)oxy]ethyl}-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 3-(1-piperazinyl)-1-[2-(2,4,5-trifluorophenoxy)ethyl]-2(1H)-pyrazinone,
 - 25 • 3-(1-piperazinyl)-1-[2-(2,3,5,6-tetrafluorophenoxy)ethyl]-2(1H)-pyrazinone,
 - 1-[2-(2,3,4,5,6-pentafluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 1-[2-(4-chloro-2-fluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 30 • 1-[2-(3-cyanophenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 1-[2-(4-cyclopentylphenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,

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- 1-[2-(1,2-benzisoxazol-3-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-methoxyphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-*n*-butyloxyphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 5 • 1-[2-([1,1'-biphenyl]-3-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 3-(1-piperazinyl)-1-[2-(2,3,4-trifluorophenoxy)ethyl]-2(1*H*)-pyrazinone,
- 1-[2-(2,3-dichlorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(1,3-benzodioxol-5-yloxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,4-difluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 10 • 1-{2-[(2-oxo-1,3-benzoxathiol-5-yl)oxy]ethyl}-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-hydroxyphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 3-(1-piperazinyl)-1-[2-(6-quinoxalinyloxy)ethyl]-2(1*H*)-pyrazinone,
- 1-{2-[3-(*N,N*-dimethylamino)phenoxy]ethyl}-3-(1-piperazinyl)-pyrazin-
- 15 2(1*H*)-one,
- 3-(1-piperazinyl)-1-{2-[3-(trifluoromethyl)phenoxy]ethyl}-2(1*H*)-pyrazinone,
- 1-[2-(3-fluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3-nitrophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 20 • 1-[2-(3-benzoylphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(3,5-difluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(phenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,6-difluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2-cyanophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 25 • 1-[2-(4-trifluoromethylphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(4-bromophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-{4-phenoxy-(phenoxy)}ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(4-fluorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 30 • 1-[2-(4-isopropylphenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2,4,5-trichlorophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,
- 1-[2-(2-methylthiophenoxy)ethyl]-3-(1-piperazinyl)-2(1*H*)-pyrazinone,

- 1-[2-(3-methoxyphenylthio)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-((4-allyl-2-methoxy)phenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(5,6,7,8-tetrahydro-naphthalen-2-yloxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,6-difluorophenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(4-trifluoromethylphenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(4-bromophenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(phenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(3-methyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1H)-pyrazinone,
- 1-[2-(4-fluorophenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1H)-pyrazinone,
- 1-[2-(4-isopropylphenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1H)-pyrazinone,
- 1-[2-(2-methylthiophenoxy)ethyl]-3-(1,4-diazepan-1-yl)-2(1H)-pyrazinone,
- 1-(2,4,5-trifluorobenzyl)-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-[3-(2,4,5-trifluorophenyl)propyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 1-(2,3-dihydro-benzo[1,4]dioxin-2-ylmethyl)-3-(1-piperazinyl)-2(1H)-pyrazinone,
- 3-piperazin-1-yl-1[2-(2,4,5-trifluoro-phenoxy)-ethyl]-1H-quinoxalin-2-one
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(4-n-butyl-1-piperazinyl)-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-[4-(2-methoxyethyl)-1-piperazinyl]-2(1H)-pyrazinone,
- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(4-methyl-1-piperazinyl)-2(1H)-pyrazinone,

✓
A QUINOLINONE
COMPOUND

- 1-[2-(2,4,5-trifluorophenoxy)ethyl]-3-(4-isopropyl-1-piperazinyl)-2(1H)-pyrazinone,
 - 1-{2-[(5-methyl[1,2,4]triazolo[1,5-a]pyrimidin-7-yl)oxy]ethyl}-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 5 • 1-[2-(4-Cyanophenoxy)ethyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 1-[4-(2,4,5-trifluorophenoxy)butyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 1-[3-(2,4,5-trifluorophenoxy)propyl]-3-(1-piperazinyl)-2(1H)-pyrazinone,
 - 3-[4-(1-phenylethyl)piperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]-pyrazin-2(1H)-one,
 - 10 • 3-[4-(2-phenoxyethyl)piperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]-pyrazin-2(1H)-one,
 - 3-[4-(2-Phenylethyl)piperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1H)-one, hydrochloride,
 - 3-(4-Benzylpiperazin-1-yl)-1-[2-(2,4,5-trifluorophenoxy)ethyl]pyrazin-2(1H)-one hydrochloride,
 - 15 • 3-[(2R)-2-methylpiperazin-1-yl]-1-[2-(2,4,5-trifluorophenoxy)ethyl]-pyrazin-2(1H)-one,
 - 3-piperazin-1-yl-1-[2-(3-thienyl)ethyl]pyrazin-2(1H)-one,
 - 3-piperazin-1-yl-1-[2-(2-thienyl)ethyl]pyrazin-2(1H)-one,
 - 20 • 1-[2-(1H-indol-3-yl)ethyl]-3-piperazin-1-ylpyrazin-2(1H)-one,
 - 1-[2-(2,3-dihydro-1,4-benzodioxin-5-yloxy)ethyl]-3-piperazin-1-ylpyrazin-2(1H)-one,
 - 1-[2-(phenylthio)ethyl]-3-piperazin-1-ylpyrazin-2(1H)-one,
 - 1-(3-oxo-3-phenylpropyl)-3-piperazin-1-ylpyrazin-2(1H)-one, or
 - 25 • 1-[3-(4-fluorophenyl)-3-oxopropyl]-3-piperazin-1-ylpyrazin-2(1H)-one,
- and their pharmacologically acceptable salts and solvates.

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LACK OF ENABLEMENT.

15 A pharmaceutical composition comprising a compound according to claim 1 as an active ingredient, together with a pharmaceutically acceptable carrier.

30

16 A method for the prophylaxis or treatment of a 5-HT_{2A} receptor-related disorder or medical condition comprising administering to a subject in need

SHOULD
SAY
"HYDRATES"

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NOT ENABLED
ANY DISORDER
THAT OCCURS IN
ANY ANIMAL THAT HAS
A 5HT_{2A} RECEPTOR

CANCEL 15,
MAKE 16 INDEPENDENT

thereof a therapeutically effective amount of a compound according to claim 1.

17 The method according to claim 15 wherein the disorder or medical condition is selected from angina; Raynaud's phenomenon; intermittent claudication; coronary or peripheral vasospasms; hypertension; ~~fibromyalgia~~; ~~thrombotic illness including stroke~~; ~~memory disorders~~; schizophrenia; obsessive-compulsive disorder; ~~mood disorders~~; autism; attention deficit hyperactivity disorder (ADHD); anxiety disorders; depression disorders including ~~depression with coexisting diabetes~~; ~~sexual function disorders~~; ~~sleep disorders~~; ~~pain~~; substance abuse; extrapyramidal symptoms; ~~Parkinson's disease~~; ~~glaucoma including normal tension glaucoma~~; ~~urinary incontinence including urinary incontinence with co-existing diabetes~~; menopausal and post-menopausal hot flushes; premenstrual syndrome; bronchoconstriction disorders; eating disorders; or ~~diabetic complications~~.

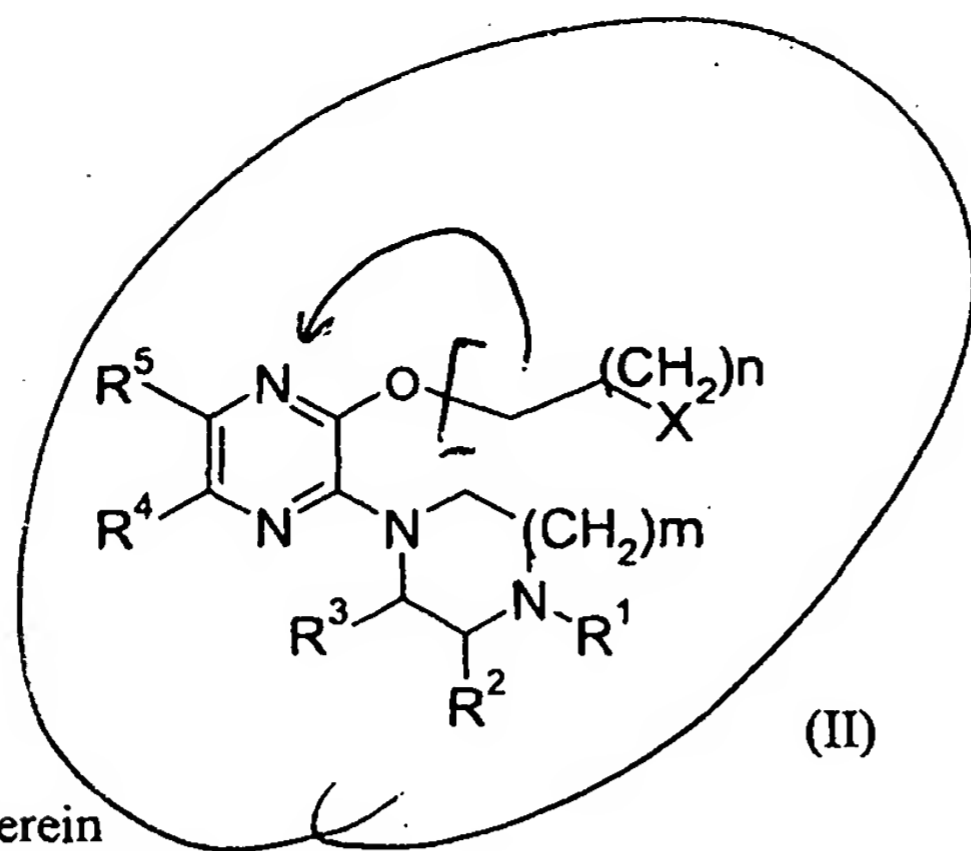
18 The method according to claim 15 wherein the disorder or medical condition is Alzheimer's disease. 11211

19 The method according to claim 15 wherein the disorder or medical condition is associated with neuroleptic drug therapy. INDEF. AND FULL SCOPE AT ENDED. "ASSOCIATED" IS ANY DES. THAT HAS

20 The method according to claim 15 wherein the disorder or medical condition is binge eating disorders, anorexia nervosa or bulimia.

21 A method for diagnosing a 5-HT_{2A} receptor-related disorder or medical condition comprising administering a radiolabelled compound of formula (I) to a test subject. LEAB. NOT COMMENTED CANCEL.

22 A method of making a compound of formula (I) according to claim 1, wherein R⁶ is selected from aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, or heteroaryl-NH, by reacting a compound of the following formula (II):



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wherein

m is 1 or 2;

n is 1 or 2;

5

X is OH;

R¹ is H, C₁₋₆-alkyl, aryl-C₁₋₃-alkyl, heteroaryl-C₁₋₃-alkyl, 2-hydroxyethyl, methoxy-C₂₋₄-alkyl, C₁₋₄-alkoxycarbonyl, aryloxy-C₂₋₃-alkyl, or heteroaryloxy-C₂₋₃-alkyl; wherein

10

any aryl or heteroaryl residue may be substituted with C₁₋₄-alkyl, C₁₋₄-alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano;

15

R² and R³ each, independently, represent H or CH₃; and

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1H-quinoxalin-2-one nucleus;

with an optionally substituted phenol or thiophenol; in a solvent.

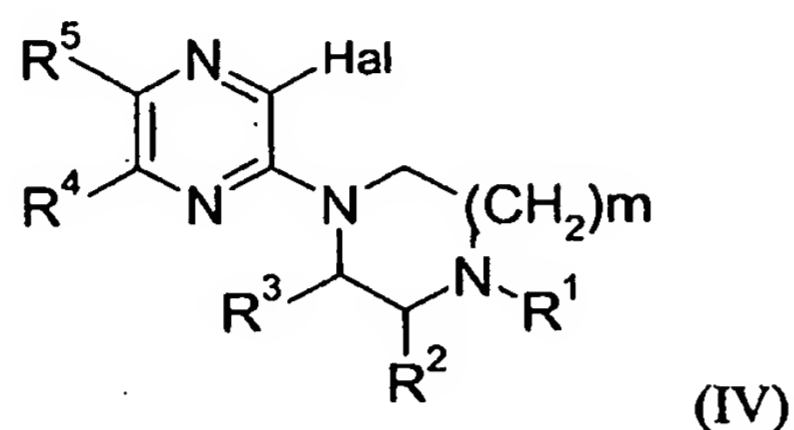
20

22. A method according to claim 21 for the preparation of compounds of formula (I) where R¹ is H, wherein R¹ in the corresponding intermediate of formula (II) is a protecting group selected from *tert*-butoxycarbonyl (*t*-BOC) or trityl.

25

21. A method according to any one of claims 21 or 22, wherein the intermediate of formula (II) is selected from:
2-[3-(4-*tert*-butoxycarbonyl-3-methyl-1-piperazinyl)-pyrazinyloxy]ethanol;
tert-Butyl (3*R*)-4-[3-(2-hydroxyethoxy)pyrazin-2-yl]-3-methylpiperazine-1-carboxylate; and
tert-Butyl 4-[3-(2-hydroxyethoxy)pyrazin-2-yl]-1,4-diazepane-1-carboxylate.

22 23 A method of preparing a compound of formula (I) according to claim 1, wherein R⁶ is selected from aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, heteroaryl-NH, aryl, arylcarbonyl, heteroaryl, or heteroarylcarbonyl, by reacting a compound of the following formula (IV),



wherein

m is 1 or 2;

Hal is halogen;

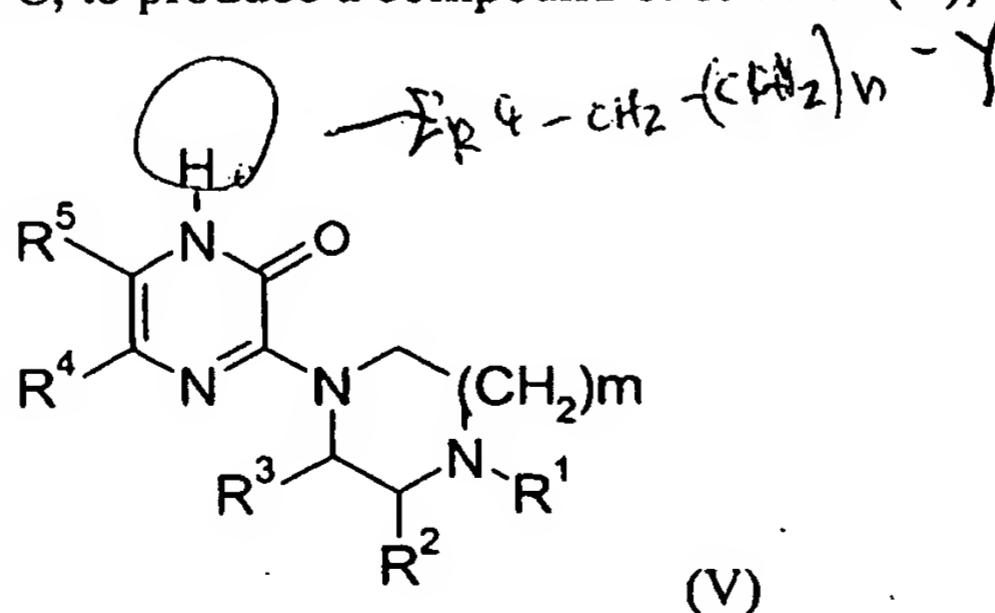
10 R¹ is H, C₁₋₆-alkyl, aryl-C₁-C₃-alkyl, heteroaryl-C₁-C₃-alkyl, 2-hydroxyethyl, methoxy-C₂-C₄-alkyl, C₁-C₄-alkoxycarbonyl, aryloxy-C₂-C₃-alkyl, or heteroaryloxy-C₂-C₃-alkyl; wherein

any aryl or heteroaryl residue may be substituted with C₁₋₄-alkyl, C₁₋₄-alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano;

15 R² and R³ each, independently, represent H or CH₃; and

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1H-quinoxalin-2-one nucleus;

20 with an alkali metal or alkaline earth metal basic salt, in aqueous media, at 25 to 150 °C, to produce a compound of formula (V),



wherein

m is 1 or 2;

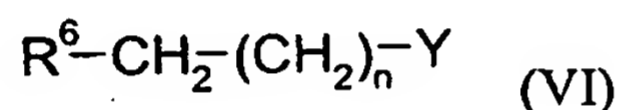
R¹ is H or C₁₋₆-alkyl, aryl-C₁-C₃-alkyl, heteroaryl-C₁-C₃-alkyl, 2-hydroxyethyl, methoxy-C₂-C₄-alkyl, C₁-C₄-alkoxycarbonyl, aryloxy-C₂-C₃-alkyl, or heteroaryloxy-C₂-C₃-alkyl; wherein

any aryl or heteroaryl residue may be substituted with C₁₋₄-alkyl, C₁₋₄-alkoxy, C₁₋₄-alkylthio, halogen, trifluoromethyl, trifluoromethoxy or cyano;

R² and R³ each, independently, represent H or CH₃; and

R⁴ and R⁵ each, independently, represent H, halogen, methyl, or together with the ring, to which carbon atoms they are attached, form a 1*H*-quinoxalin-2-one nucleus;

followed by N-alkylation of the compound of formula (V) by reaction with a compound of formula (VI),



wherein

n is 0, 1, 2, 3 or 4;

Y is a leaving group; and

R⁶ represents aryloxy, heteroaryloxy, arylthio, heteroarylthio, aryl-NH, heteroaryl-NH, aryl, arylcarbonyl, heteroaryl, or heteroarylcarbonyl; and

wherein any aryl or heteroaryl residue, alone or as part of another group, may be unsubstituted or substituted. Where substituted, one, two, three, four or five substituents may be present, preferably one or two for non-halogen substituents, and are independently selected from aryl, aryl-C₁₋₂-alkyl, arylcarbonyl, heteroaryl, heteroaryl-C₁₋₂-alkyl, heteroarylcarbonyl, aryloxy, heteroaryloxy, arylthio, heteroarylthio, arylamino, heteroarylamino, C₃₋₆-cycloalkyl, C₃₋₆-cycloalkyloxy, C₃₋₆-cycloalkylcarbonyl, C₁₋₆-alkyl, C₂₋₆-alkanoyl, C₂₋₆-alkynyl, C₂₋₆-alkenyl, or fluoro-C₂₋₄-alkyloxy, halogen, trifluoromethyl, nitro, cyano, trifluoromethoxy, trifluoromethylthio, C₁₋₆-alkoxy, C₁₋₆-alkylthio, C₁₋₆-alkylamino, C₁₋₄-dialkylamino, hydroxy or oxo;

wherein any aryl or heteroaryl residue as substituents
on aryl or heteroaryl, alone or as part of another group, in turn
may be substituted in one or more positions, preferably one,
independently of each other by C₁₋₄-alkyl, C₁₋₄-alkoxy, C₁₋₄-
alkylthio, halogen, trifluoromethyl, trifluoromethoxy, or
cyano;

in the presence of a base in a suitable solvent at an elevated temperature.

25. A method according to claim 24 for the preparation of compounds of formula
(I) where R¹ is H, wherein R¹ in the corresponding intermediate of formula
(V) is a protecting group selected from tert-butoxycarbonyl (t-BOC) or trityl.

26. The method according to claim 22 wherein R¹ in the corresponding
intermediate of formula (II) is tert-butoxycarbonyl (t-BOC).

27. The method according to claim 25 wherein R¹ in the corresponding
intermediate of formula (V) is tert-butoxycarbonyl (t-BOC).

28. The compound according to claim 1 where in the compound of formula (I)

20 13 n = 1;

R¹ is aryl-C₁-C₃-alkyl;

R², R³, R⁴ and R⁵ are each H; and

R⁶ is 2,4,5-trifluorophenoxy.